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Coming Meetings

The American College of Physicians, Postgraduate Course, Special Topics in Internal Medicine, University of Colorado School of Medicine, Denver, June 15-19, 1959.

University of Colorado Medical Center, Fifth Annual Postgraduate Course, Dermatology for General Practitioners, Denver, July 16-18, 1959.

Postgraduate Medical Assembly of South Texas, Annual Meeting, Shamrock Hilton, Houston, July 20-22, 1959.

New Mexico Academy of General Practice, Summer Clinic, Ruidoso, N. Mex., July 20-23, 1959.

Rocky Mountain Cancer Conference, Brown Palace Hotel, Denver, July 22-23, 1959.

Nevada State Medical Association, Annual Meeting, Mapes Hotel, Reno, Aug. 19-22, 1959.

American Fracture Association, Annual Meeting, New Orleans, Nov. 1-3, 1959.

Southwest Obstetrical and Gynecological Society, Annual Meeting, El Mirador Hotel, Palm Springs, Calif., Nov. 2 and 3, 1959.

Southwestern Medical Association, Annual Meeting, Roswell, N. M., Nov. 5-7, 1959.

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SOUTHWESTERN MEDICINE

VOL. XL JUNE, 1959 No. 6

Syphilis—Current Status of Diagnosis

By MAURICE R. VINIKOFF, M.D., Director V. D. Division, El Paso City-County Health Unit*

I have been asked to prepare three simple articles as a guide to the diagnosis, treatment, and follow-up of syphilis for the average physician. By necessity, these will be brief and definitive, giving more or less the procedures followed at the venereal disease clinic of the City-County Health Unit of El Paso.

Variations in schedules, other drugs and procedures, etc., will be purposely excluded for simplicity. The first article will deal with the diagnosis of syphilis. Although the history and physical examination are stressed in the diagnosis of all diseases, one may tend to pass over the elements when supposedly adequate diagnostic laboratory techniques are available. In syphilis, however, one cannot stress too greatly the importance of the history and physical examination, especially in the presence of conflicting and inconclusive laboratory reports.

Factors Emphasized

Factors in the history which are emphasized are:

1. History of signs and symptoms of syphilis and their duration.

2. History of previous anti-syphilitic treatment per se or prolonged antibiotic therapy which might affect the serologic study.

3. Results of pregnancies in the female with special reference to late abortion, stillbirth, etc. This is a frequent occurence in syphilitic patients.

4. History of syphilis in the family (congenital syphilis) or sex contacts would tend to substantiate an otherwise doubtful case.

5. History of recent illness or immunization which might cause a biologic false positive reaction.

6. Results of previous serologies are beneficial in determining the duration of the disease as well as correlating these reports with previous serological results.

Physical Examination

Factors in the physical examination which are emphasized:

1. Careful examination of the skin and mucosa for signs of lesions as well as lymph node enlargement.

2. Eyes are examined for evidence of Argyle-Robertson Pupils, muscle imbalance, Keratitis, etc.

3. Signs of congenital syphilis are looked for such as the teeth which are checked for mulberry molars or Hutchinsons teeth. Saddle nose, saber shins, joint swellings, etc., should all be borne in mind.

4. Cardiovascular system is checked for evidence of aortic insufficiency, aortitis, aneurysm of the aorta, coronary ostial stenosis, etc.

5. The abdomen is examined for splenomegaly or hepatomegaly.

6. Complete neurological examination is made including Romberg test, deep reflexes, cranial nerves, etc., with special attention to signs of tabes dorsalis, paresis, transverse myelitis, etc.

Laboratory Examinations

The ultimate in the diagnosis is the isolation of treponema pallidum from available lesions such as

CURRENT THERAPY

*Dr. Vinikoff this month is substituting for Dr. Jack A. Bernard, regular conductor of this section.

the primary chancre or by lymph node aspiration and their identification by the darkfield technique. The secondary mucous membrane or skin lesions abound with spirochetes. It should be borne in mind however that the administration of antibiotics even in relatively small doses will affect the presence of treponema in the above lesions. However, the diagnostic problems in syphilis are not those connected with the above types of lesions.

In the absence of lesions a positive history or physical examination with reference to the factors noted above plus a laboratory positive serologic test for syphilis is considered adequate for the establishment of a diagnosis of syphilis. The serologic tests most widely used at the present time are VDRL, Kahn, Eagle, and the Kolmer; although any other standard tests are acceptable.

Repeat Serology

In the presence of a completely negative history and physical, and with a positive serology, one should always repeat the serology and preferably have both a precipitation test such as the VDRL, Kahn, or Eagle performed, as well as a complement fixation test such as the Kolmer. If the tests are confirmatory and of fairly high titre, one is justified in making a diagnosis of syphilis and initiating therapy.

In the low titre or doubtful reactors or in the case of conflicting serologic reports, one should always perform a spinal fluid examination. A positive spinal fluid reaction to the standard tests is reasonably confirmatory evidence of syphilis since biologic false positive reactions from spinal fluids are extremely rare or non-existent.

In the presence of a negative history, physical, and spinal fluid, with low titres or conflicting reports, the use of treponemal tests are of inestimable value.

Tests Specific

These tests are for all practical purposes specific. Biologic false positive tests resulting from the collagen diseases, vaccination, mononeucleosis, do not occur. The treponema pallidum immobilization test, commonly referred to as the T.P.I. test, is extremely popular at this time. The cost (approximately $30) limits its general use and its performance requires great technical skill and material.

The Reiter protein complement fixation test (RPCF) is another treponemal test which can be run by any laboratory equipped for complement fixation tests and should cost about $5. This test compares very favorably with the T.P.I. test and is now being performed at many state and private laboratories. The antigen is available commercially.

In the doubtful and problem cases, the T.P.I. or R.P.C.F. tests, can be used to help confirm or exclude a diagnosis of syphilis. It is hoped that in the near future these or similar tests will be available generally and possibly replace the non treponemal reagin tests now in use.

Dr. Schuessler New Head of Texas Plastic Surgeons

Dr. Willard W. Schuessler, Past President of the Southwestern Medical Association, was elected President of the Texas Society of Plastic Surgeons at its annual meeting during April in San Antonio.

Dr. Schuessler, who recently completed a year as President of the El Paso Chamber of Commerce, is a diplomate of the American Board of Plastic Surgeons, a Fellow of the International College of Surgeons, and a member of the American Association of Plastic Surgeons, the American Society of Plastic and Reconstructive Surgeons, The Texas Surgical Society and the founder group of the Southwestern Surgical Congress.

MEETINGS

Dr. Cameron

Dr. David M. Cameron of El Paso Elected President of Texas Orthopaedic Association

Dr. David M. Cameron of El Paso was elected President of the Texas Orthopaedic Association at its annual meeting in San Antonio April 20. He succeeds Dr. Louis J. Levy of Fort Worth.

Other Officers

Other new officers are Dr. Gerald S. Ahern, Corpus Christi, Vice-President; and Dr. Margaret Watkins, Dallas, Secretary-Treasurer, who was re-elected to the post.

The Association voted to hold its 1960 meeting in Fort Worth in conjunction with the annual session of the Texas Medical Association, as it did this year in San Antonio.

Speakers

Speakers were Dr. Lenox D. Baker, Professor of Orthopaedic Surgery, Duke University, Durham, N. C.; Dr. Edward L. Compere, Professor and Chairman of the Department of Orthopaedic Surgery, Northwestern University Medical School, Chicago; Dr. E. Burke Evans, Galveston; Dr. Herbert Hipps, Waco; Dr. Paul Harrington, Houston; Dr. Louis J. Levy, Fort Worth; Lt. Col. J. J. Brennan, William Beaumont Army Hospital, El Paso.

Dr. J. H. Cherry, Galveston; Dr. C. F. Gregory, Dallas; Col. E. W. Brannon, Lackland Air Force Base Hospital, San Antonio; Dr. H. H. Brindley and Dr. Warren A. Ross, both of Temple.

Dr. Cameron was born Sept. 20, 1910, in Joplin, Mo. He moved with his family to El Paso in 1918 and attended local schools. He was a student at Texas College of Mines, now Texas Western College, from 1927 to 1929 and transferred to the University of Arizona from which he received a B. A. degree in 1931.

Graduated From University of Texas

He was graduated from the University of Texas Medical Branch at Galveston in 1935 and was an

interne at John Sealy Hospital during 1935 and 1936. He was a surgical interne at the University of Minnesota Hospitals in 1936 and 1937 and took postgraduate work from the University of Minnesota at Mayo Clinic, where he was a Fellow in Orthopaedic Surgery, from 1937 to 1940.

He began private practice in El Paso in 1940 in partnership with Dr. Frank Goodwin. He entered service as a Captain in 1942 and served in the American and European Theaters of Operation before his discharge as a Lieutenant Colonel in 1946. He resumed his private practice in El Paso the same year.

He is a Diplomate of the American Board of Orthopaedic Surgery, a Fellow of the American College of Surgeons and a member of the El Paso County Medical Society, Southwestern Surgical Association, Texas Medical Association, American Medical Association, Clinical Orthopaedic Society, Western Orthopaedic Association, Southwestern Surgical Association and Texas Orthopaedic Association. He is a founding member of the Southwestern Medical Association.

Dr. Cameron is an active staff member of Southwestern General Hospital and courtesy member of the staffs of Hotel Dieu, Providence Memorial Hospital and El Paso General Hospital.

He is a former consultant to the Surgeon General at William Beaumont Army Hospital.

He is a member of Los Caballos, the Sheriff's Posse, and the El Paso Country Club.

Married, he and his wife have three children: Ann, 13 and twin sons, David and Don, 11. The family home is at 4700 Hastings Street.

AT TEXAS ORTHOPAEDIC MEET — Among those present at the annual meeting of the Texas Orthopaedic Association in San Antonio April 20 were, left to right, Col. E. W. Brannon, Lackland Air Force Base Hospital, San Antonio, one of the speakers; Lt. Col. J. J. Brennan, William Beaumont Army Hospital, El Paso, a speaker; Dr. E. Burke Evans, Galveston, a speaker; Dr. Elias Margo, Oklahoma City, an orthopaedic surgeon who was in San Antonio for the 40th reunion of his class of 1919, graduated from the University of Texas Medical Branch at Galveston; and Dr. Gerald S. Ahern, Corpus Christi, new Vice-President of the Association.

New Mexico Academy of General Practice
Ruidoso Summer Clinic

July 20-23, 1959

MONDAY, July 20
9:00-10:30 A.M.

Three lectures on "Steroids"
"USES," by Dr. Alfred J. Leiser, Internist, Houston
"COMPLICATIONS," by Dr. James Kemper, Rheumatology, Houston
"IN DERMATOLOGY," by Dr. H. D. Garrett, El Paso

10:45 A.M.-12:15 P.M.

Panel — "Steroids Today"

12:30-2:00 P.M.

Luncheon and New Mexico Chapter Business Meeting

TUESDAY, July 21
9:00-10:30 A.M.

Three features on "Psychosomatic Medicine"
Dr. Alfred Leiser, Internist, Houston
Dr. James Kemper, Rheumatology, Houston
Dr. Warren Brown, Psychiatrist, Albuquerque
or
Dr. H. F. Ford, Psychiatrist, Galveston

10:45 A.M.-12:15 P.M.

Panel — "Psychosomatic Medicine"
Drs. Leiser, Kemper, Brown and Ford

12:30-2:00 P.M.

Luncheon and question period for above four speakers

WEDNESDAY, July 22
9:00-9:30 A.M.

"Common Fractures in General Practice"
by Dr. Arthur Glassman, Orthopedist, Houston

9:30-10:00 A.M.

"Office Gynecology"
by Dr. Stanley Roger, Obstetrician-Gynecologist, Houston

10:00-10:30 A.M.

"Diagnosis and Management of Kidney Colic"
by Dr. Abel J. Leader, Urologist, Houston

10:45 A.M.-12:15 P.M.

Panel — "Low Back Pain"
by Drs. Glassman, Roger, Leader, and Dr. E. K. Neidich, Radiologist, Las Cruces, N. M.

12:30-2:00 P.M.

Luncheon and question period for above speakers

THURSDAY, July 23
9:00-9:30 A.M.

"Management of Orthopedic Difficulties of the Newborn" by Dr. Glassman

9:30-10:00 A.M.

"Evaluation of Cephalo-Pelvic Disproportion"
by Dr. Stanley Roger

10:00-10:30 A.M.

"Management of Urinary Tract Infection"
by Dr. Abel Leader

10:45 A.M.-12:15 P.M.

These presentations are made possible by a grant from MERCK, SHARPE AND DOHME Post Graduate Program.

NO AFTERNOON SESSIONS

How high will the social security tax go? No one knows. But in South America some countries are paying tax rates as high as 25% of payroll. In France, the tax rate is 35% of much of their payroll and is one of the principle reasons for the failure of the French economy to make a postwar comeback.

ORTHOPAEDIC SURGERY NOTES

Avulsion Injuries of the Posterior Cruciate Ligaments*

By JOHN J. BRENNAN, LT COL, MC, U.S.A.,
William Beaumont Army Hospital, El Paso

Avulsion fractures of the tibial attachment of the posterior cruciate ligament occur as isolated injuries infrequently. In some cases with minimal displacement of the fragment a satisfactory result can be obtained by conservative measures. In severe cases subluxation of the knee or displacement of the bony fragments may necessitate open reduction.

A difference of opinion concerning the importance of the cruciate ligaments for normal knee function and the necessity of their repair is evident in medical literature of the past. Milch[1] reports that: "Where the cruciate or collateral ligaments have been injured, repair of the tibial collateral ligament alone has been sufficient to restore an excellent functional capacity in the unstable knee.

Cruciate Ligament

The more complicated cruciate ligament reconstruction does not seem to have justified itself while the importance of the tibial collateral ligament cannot be denied." Bristow,[2] Hey Groves, [3,4] Gallie and Le Mesurier,[5] regarded the cruciate ligaments as the important stabilizers of the knee. Saunders,[6] and Milch believed that rupture of the anterior cruciate ligaments resulted in no instability of the knee.

Hey Groves[3] believed rupture of the cruciate ligaments gives a permanently disabled knee. Gallie and Le Mesurier[5] believed rupture of the posterior cruciate ligament invariably gives an unstable knee. Brantigan and Voshell[7] reported backward gliding of the tibia on the femur in extension, which increased in flexion, when the posterior cruciate ligament was cut.

In stripped joints the movement is increased, and in flexion the lateral femoral condyle tends to rock off the tibial condyle when the collateral ligaments are intact and the cruciate ligaments are cut. This anterior-posterior motion is increased in the fresh joint and if rotation is permitted the abnormal motion is greater.

The posterior capsule and soft structures of the knee prevent the femoral condyle from rocking off of the tibia in the fresh joints. The controversy over the need to repair injured cruciate ligaments has been concerned mainly with the need for repair of the torn anterior cruciate ligament, and not so much with the torn posterior cruciate.

Unusual Situations

Voshell stated: "In the presence of a good tibial collateral ligament, and well-trained muscular structures, the injured anterior cruciate need not be repaired except under unusual economic or athletic situations. The tibial collateral ligament is the most important single ligament of the knee, but even it is dependent upon the efficiency of one or both cruciates, especially the posterior."

Cubbins, Callahan and Scuderi[8] felt that early operation for the rupture of a single ligament is always indicated and that results are much better if the operation is performed at an early date. O'Donaghue[9,10] has more recently revived our interest in early surgical repair of ligament injuries of the knee.

Many operations have been reported for repair or reconstruction of isolated ligament injuries in the knee, but few for repair of the torn posterior cruciate ligament. Most of these are applied to older injuries in reconstructive attempts to replace the function of the ligament by means of tendon or fascial grafts.

Lee[11] reported a surgical method of reduction of the avulsed bone fragment of the attachment of the anterior cruciate ligament. The fragment is secured by wire passing through drill holes in the anterior tibia where the wire is drawn tight and tied. He approached the avulsion fracture of the posterior cruciate attachment through a posterior approach in the popliteal space.

Sutures to the capsule were used to fix the bony fragment in place. Wire fixation to the tibia was not used. Abbott, et. al.[6] repaired the avulsion fracture through a popliteal incision. They fixed the bony attachment into the defect on the posterior rim of the tibia by a screw or sutures.

This posterior approach is rather formidable and limits the operator to a limited view of the

*Presented at the Annual Meeting of the Texas Orthopaedic Association in San Antonio, Texas on April 20, 1959.

posterior of the joint. Associated pathology in the anterior of the knee joint must be approached through an extra anterior incision. Without this, anterior pathology in the knee could be missed.

Method of Repair

The purpose of this report is to present a method of repair of the posterior avulsion fracture by means of a simpler posteromedial incision combined with an anterior incision. By this method the technique employed by Lee for the repair of the anterior cruciate ligament is used for the repair of the posterior cruciate avulsion injury.

The Operation: The patient is positioned supine on the operating table. A pneumatic tourniquet is inflated on the thigh. With the knee flexed at 155 degrees a conventional small anteromedial vertical parapatellar skin incision is made and the knee entered in the conventional manner. The anterior portion of the knee joint is inspected from this incision.

Th presence of injury to the anterior cruciate ligament, the medial meniscus and the deep portion of the medial collateral ligament can thus be detected through this incision. When the anterior pathology is fully excluded or apparent to the operator, he proceeds to the posteromedial incision.

Posterior Incision

The posterior incision is vertical and prolonged upwards and downwards from the same type incision as usually employed for posterior approach to the meniscus or drainage of the joint as described by Henderson.[12,13] Bristow[2] reports the late Alwyn Smith of Cardiff was the first surgeon to his knowledge to use this incision for removal of the posterior portion of the meniscus.

This incision is usually five to six inches in length. The incision is developed anterior to the semimembranosis and semitendinosis tendons. The saphenous nerve is protected. The joint capsule is entered by a vertical incision, exposing the posterior compartment of the knee. The avulsion fracture becomes apparent and the loose comminuted bone fragments can be removed. The medial semilunar cartilage is completely removed through the anterior and posterior incisions.

This increases the visibility greatly in the posterior compartment of the knee. The medial tibial periosteum is incised and the posterior medial cortex of the tibia is exposed. Two drill holes are made from this cortex to the posterior defect of the tibia. These should preferably be placed in the outer lateral and medial portion of the defect.

Stainless steel wire suture is passed through one hole. This is then passed over the bony fragment and through its ligament attachment. The wire is then passed out through the second drill hole. Forward displacement of the tibia on the femur facilitates reduction of the fragment.

Anterior Cruciate

The anterior cruciate ligament laxity can be checked through the anterior incision to be sure of optimum tension. When the wire is made taut and tied the reduction is made fast and the optimum tension of the associated ligament is assured. The incisions are then repaired by sutures in a conventional manner. Sterile dressing and a long leg cast are applied for immobilization.

Postoperative Care: Active quadriceps activity is started the second postoperative day. Cast immobilization is continuous for four to six weeks. After discontinuing cast immobilization the patient is not permitted full weight bearing until extension of the knee of 170 to 180 degrees is possible.

Two cases are herein reported. In the first case damaged skin of the popliteal area of the knee necessitated this approach to repair the avulsion fracture. In both cases damaged medial menisci were found justifying the removal of the meniscus which facilitated surgical exposure of the posterior compartment and made this type of repair possible.

Case 1.—This 26-year-old male was injured in an automobile accident on May 12, 1952. He was admitted to a nearby civilian hospital with a severe head injury and in a semicomatose condition. A large laceration of the right frontal region of the scalp required sutures. His condition was critical, but his sensorium began to improve on May 16.

The patient was transferred to the United States Army Hospital, Camp Gordon, Ga. on May 20, 1952. Upon admission the patient showed dysmetria of the right lower face. He was confused and disoriented but reacted to painful stimuli. His left knee was swollen and painful. He resisted all efforts to move the knee.

The patient's roentgenograms showed negative skull and sinus films. The pneumoencephalogram was within normal limits. Roentgenograms of the left knee showed an avulsion fracture of the tibia at the attachment of the posterior cruciate ligament. (Fig. 1A). Slight posterior subluxation of the knee was present. The skin of the popliteal area was macerated, abraded and weeping.

The patient was treated with skin traction to the left leg. The knee failed to straighten or improve. The lesions of the skin in the popliteal area healed and his mental status slowly improved.

Arthrotomy Performed

On June 12, 1952, an arthrotomy of the left knee was performed. A posteromedial skin incision, six inches in length, was employed. The fractured fragment of the posterior tibia was found attached to the posterior cruciate ligament and displaced upward. The fractured fragment was intact and not comminuted. The view of the pathology was somewhat limited. The medial meniscus was found torn loose in its posterior portion.

A second anteromedial parapatellar incision was made and the meniscus was removed using both incisions. Through this second incision the anterior cruciate ligament was found intact but lax. The granulation tissue was then gently cleaned from the fracture defect through the posterior incision. The fractured fragment could be reduced into the defect when the tibia was displaced forward to make the anterior cruciate ligament taut.

Cortex of Tibia Exposed

The posteromedial cortex of the tibia was then exposed. A drill was passed through this cortex to emerge at the margins of the bone defect. A wire suture was passed through one hole, then through the bone fragment and the posterior cruciate ligament, and returned through the second hole to the outer cortex.

Traction applied to this wire adequately reduced and held the fractured fragment in position. This was secured by tying the wire and the ends of the wire were turned into a drill hole. (Fig. 1B). The wounds were closed and a plaster of paris cast was applied as immobilization.

Limb Immobilized

The patient's limb was immobilized for six weeks. His rehabilitation was slow because of his head injury. His mental status slowly improved, permitting him to return to a limited duty status on November 5, 1952. The patient had knee motion of 170 degrees to 90 degrees and walked with a slight limp. His knee showed good stability.

This case was complicated by slow recovery from a severe head injury and slow recovery of the injured knee. This experience, however, convinced the author that the method of Lee as used for repair of avulsion fractures of the anterior cruciate ligament could be applied through a posteromedial approach to avulsion fractures of the posterior cruciate ligament attachments. For this reason, this method was used in the following case.

Case 2.—This 26-year-old male was transferred to William Beaumont Army Hospital on March

Figure 1, Case 2. (A) Roentgenogram showing avulsion fracture, posterior tibial spine with displacement upwards and with posterior subluxation of tibia on femur. (B) Anteroposterior view of the same knee.

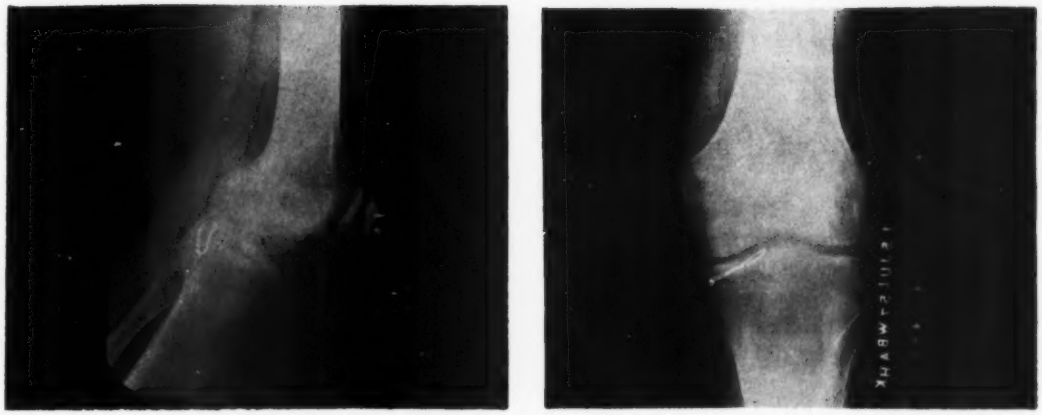

Figure 2. (A) Post-operative lateral roentgenogram revealing the wire suture and facture in position. (B) Anteroposterior view of same case after fixation through Henderson posteromedial approach.

25, 1957. He was injured in a motorcycle accident on March 22, 1957. He had injured his left knee and his right ankle. Roentgenograms revealed an oblique fracture of the distal fibula at the right ankle. In the left knee an avulsion fracture of the posterior tibial spine was present with displacement upward, and with posterior subluxation of the tibia on the femur. (Fig. 2A).

Vertical Incision

On March 27, 1957, a vertical six inch posteromedial incision was made at the left knee. The synovium of the knee joint was entered and the incision was enlarged proximally and distally. A bony defect of the posterior tibia where the cruciate ligament attached was found. The visibility was poor and this necessitated removal of the medial meniscus. An added four inch median parapatellar incision was used to remove the meniscus. Drill holes in the tibia and wire suture were used to replace and retain the fractured fragment of the tibia into the posterior defects. (Fig. 2B). The incisions were closed and a long leg cast was applied.

The immobilization was discontinued May 6, 1957, five weeks postsurgery. He required wedging cast treatment to regain full extension of the knee in July 1957. The knee showed motion of 175 degrees to 80 degrees and the knee was stable. The patient's rehabilitation progressed satisfactory and he was discharged from the hospital August 30, 1957. The patient's occupation was that of a pilot. He was returned to full flying status October 11, 1957.

Conclusions: Two cases are reported of avulsion fractures of the posterior cruciate ligament attachment of the upper tibia. These cases were approached surgically through a posteromedial incision at the knee.

The method of wire fixation of the avulsion fractures of the tibial attachment of the anterior cruciate ligament can be employed successfully in avulsion fractures of the attachment of the posterior cruciate ligaments through the posteromedial incision. Visibility is increased greatly in this procedure by removal of the medial meniscus.

The use of an anterior incision helps to secure the optimum tension of the fracture reduction as judged by tension of the anterior cruciate ligament. This incision also enables the surgeon to exclude or repair anterior lesions of the knee if they are present.

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ORIGINAL ARTICLES

Disseminated Coccidioidomycosis Treated with Amphotericin B

By Robert C. Hunter, Jr., *Colonel, MC, USA*
and Edward S. Mongan, *M.D., William Beaumont Army Hospital, El Paso*

The Essayist, Colonel Robert C. Hunter, M. C., U.S.A., and the Editor, of Medical Technicans Bulletin of the United States Armed Forces Medical Journal, Col. Robert J. Benford, M. C., U.S.A., have kindly allowed SOUTHWESTERN MEDICINE to reprint this article. This article is of particular interest to the readers of SOUTHWESTERN MEDICINE because coccidioidomycosis is endemic in this area. Colonel Hunter makes the statement that "Amphotericin B in all probability represents the first real advance in the treatment of disseminated coccidioidomycosis but further clinical testing will be essential." Those of us in the Southwestern area who have had experience with disseminated coccidioidomycosis will read and obtain benefit, I am quite sure, from this paper. SOUTHWESTERN MEDICINE wishes to thank Colonel Hunter and Colonel Benford for the privilege of reprinting this essay. **L.C.F.**

Since amphotericin B became available to us more than a year ago, we have had under observation, at this hospital, nine patients with disseminated coccidioidomycosis. Five were eliminated from the study; two because they had already undergone a clinical and serologic remission, one because he was improving rapidly when the diagnosis was established, one because he had only serologic evidence of dissemination, and one because he had far-advanced disease and died the day of admission. This report describes the results obtained in the treatment of the remaining four patients with amphotericin B.

Amphotericin B

Amphotericin B is an antibiotic derived from a species of Streptomyces found in a soil sample from the Orinoco River basin in Venezuela. In vitro, it has been shown to have antifungal properties for a wide variety of organisms, including *Coccidioides immitis.* In vivo, it has had an ameliorating effect on mice experimentally infected with C. *immitis.* In neither animals nor humans was there significant toxicity when the drug was given orally, possibly because of its poor absorption from the gastrointestinal tract.

The LD_{50} for intravenous administration in mice was 8 mg per kg. All of the mice that died did so within nine minutes of the infusion with symptoms of ataxia, spasms, and terminal collapse.[1] Littman, Horowitz, and Swadey[2] described one patient who received 28 mg. intravenously in 40 minutes. He had convulsions and cardiac standstill, but recovered. Anorexia, nausea, vomiting, chills, and fever have occurred commonly during, and shortly after, intravenous administration. Such reactions may have been minimized by use of salicylates and antihistamines. On prolonged intravenous administration there was a tendency for the blood urea nitrogen to increase, but this has subsided with temporary interruption of therapy.

The poor absorption of amphotericin B given by mouth has led to preference for the intravenous route of administration. The toxicity has necessitated slow infusion and limited dosage. It is currently recommended that the water-soluble salt be dissolved in sterile 5 per cent dextrose in water to a concentration of 1 mg. per 10 ml. The solution should be infused slowly intravenously over a period of six hours or more to a maximum dose of 1 mg. per kg. daily.[1] Littman, Horowitz, and Swadey[2] suggested a maximum dose of 1.6 mg. per kg, and believed that infusion on alternate days reduced the chances of nitrogen retention.

Lehan and associates[3] stated that in several instances when administered intravenously, the amphotericin B infiltrated into surrounding subcutaneous tissue. Mild discomfort and redness at the site resulted, but the complication was not serious. Littman, Horowitz, and Swadey repeatedly injected amphotericin B into a knee severely involved with coccidioidomycosis. The drug was well tolerated and appeared to benefit the knee.

The acute pulmonary form of coccidioidomyco-

sis is generally a benign, self-limited disease. It offers no serious therapeutic problems although it produces prolonged morbidity at times. Occasionally, a residual granuloma or cavity in the lung requires surgical removal, but the majority of these are asymptomatic and yield to expectant treatment.

The disseminated disease is relatively rare and far more serious, with a mortality of about 50 per cent. In the past 30 months we have treated 14 patients with disseminated coccidioidomycosis with five deaths to date. In one, the course was fulminating and death occurred two weeks after the onset.[4] Others have recovered spontaneously.[5] Still other have followed a chronic and slowly progressive downhill course.

Evaluation of the therapy of disseminated coccidioidomycosis has been difficult because of the irregular course of the disease. The literature has been contradictory on the subject. However, there has been no good evidence that any therapeutic agent in the past has favorably influenced the course of disseminated coccidioidomycosis.[2, 6] To the long list of ineffective agents we have added chloroquine diphosphate. We had two patients who recovered following the use of chloroquine. Our initial enthusiasm was properly curbed when this drug clearly accomplished nothing for the next seven patients with the disseminated disease.

The collection of clinical data on the therapeutic trial of amphotericin B for disseminated coccidioidomycosis has been slow. There has been little upon which to draw conclusions. Klapper, Smith, and Conant[7] and Fiese[8] each reported one case in which apparent benefit resulted from the oral administration of amphotericin B. Littman, Horowitz, and Swadey[2] reported two cases in which improvement coincided with intravenous amphotericin B. Preliminary reports to the Squibb Institute for Medical Research[1] included four additional cases, two on oral therapy and two on intravenous therapy. The results were encouraging.

Case Reports

Case 1. A 34-year-old Negro was admitted to this hospital on 10 December 1956, complaining of chest pain. About one month earlier he had noted the onset of fever, malaise, easy fatigability, shortness of breath, right-sided pleuritic type pain, cough, and occasional hemoptysis. He had been stationed in El Paso for six months in 1950, and again for nine months prior to admission.

On examination he appeared well developed, well nourished, and in no distress. His height was 70 inches; weight, 215 lb; temperature, 98.0°F; pulse, 80; blood pressure, 120/82 mm Hg. There was slight dullness and decreased breath sounds over the right lung base posteriorly. Roentgenograms of the chest showed scattered nodular densities in the left lung, an infiltration in the right lung base, and right hilar lymphadenopathy.

The white blood cell count was 11,600 per μl, with 26 per cent eosinophils. The hemoglobin 13.5 grams per 100 ml. *C. immitis* was cultured from the sputum. Reaction to the coccidioidin skin test was positive. Complement fixation for coccidioidomycosis was positive in a titer of 1:64.

One month after admission a 3- by 6-cm mass of lymph nodes was noted in the right supraclavicular area. A specimen for biopsy showed a granulomatous reaction with numerous giant cells containing thick-walled spherules and endospores. Culture of the material was positive for *C. immitis*. An abscess appeared at the biopsy site, and culture of the pus was positive for *C. immitis*. A draining sinus persisted in this area for three months, after which it healed spontaneously.

In March 1957 a coccidioidal abscess developed in the middle phalanx of the fourth toe on the patient's left foot. This was incised and drained. The resulting sinus healed about a month later.

During the first two months in the hospital the patient's general condition remained good, but he lost 35 lb. in weight. By early June, his infection appeared to be under control. A roentgenogram of his chest was clear and there was no evidence of active lesions. On 6 June therapy with amphotericin B by mouth was initiated, the patient receiving approximately 5 grams daily for 38 days. The drug was well tolerated.

His complement fixation for coccidioidomycosis was 1:16 on 27 June, and 1:8 on 5 July. He was discharged to duty on 7 August.

On follow-up examination on 13 February 1958, he appeared well. Blood cell count and roentgenographic findings of the chest were normal. His complement fixation was 1:4.

Comment

This patient was on the road to recovery when treatment with amphotericin B was started. There was no reason to believe that the drug altered the course of his disease.

Case 2. A 40-year-old Negro was admitted to this hospital on 28 January 1957, complaining

of malaise and cough. For the preceding two weeks he had had low-grade fever, night sweats, headache, malaise, and cough productive of small amounts of yellow sputum. He had been stationed in El Paso for two and one-half years.

Examination revealed a somewhat obese man who was not in acute distress. His height was 69 inches, weight, 200 lb.; temperature, 99.1°F; pulse, 88; and his blood pressure was 125/75 mm Hg. There were dullness and fine rales over the right lung base posteriorly. There was a single 3-mm granuloma in the skin of the dorsum of the right wrist. A roentgenogram of the chest showed a pneumonitis in the right lung base and right hilar lymphadenopathy.

The white blood cell count was 7,500 per μl, with 14 per cent eosinophils. The hemoglobin was 13.5 grams per 100 ml. Coccidioidin skin tests were negative throughout the course of his disease. *C. immitis* was cultured from his sputum. Complement fixation for coccidioidomycosis was negative.

About one month after admission a hard mass was noted in the right supraclavicular area. It gradually increased in size and became fluctuant. On 5 April it was incised. *C. immitis* was recovered from the pus. Three months after admission the patient had lost about 30 lb. in weight, his complement fixation for coccidioidomycosis had become positive in a titer of 1:256, and numerous new granulomata had appeared in the skin. *C. immitis* was identified microscopically and by culture in several of the skin lesions. The granulomas tended to break down leaving indolent ulcers, 1 to 3 cm in diameter, draining bloody purulent material (fig. 1).

Six months after admission the patient's condition stabilized. He regained his normal weight and appeared healthy with the exception of the ulcerations of his skin. His complement fixation had dropped to 1:64. A roentgenogram of the chest showed no change since admission.

In September, nine months after admission amphotericin B was started, 45 mg intravenously every other day. The patient regularly had chills, fever, and vomiting during and up to 12 hours after administration of the drug. In November, treatment was discontinued for two weeks because of elevation of his blood urea nitrogen. Between 22 September and 18 December he received a total of 1,125 mg of amphotericin B.

While on therapy all of his skin lesions healed, roentgenographic finding of his chest became normal, and his complement fixation dropped from 1:64 to 1:8. He was discharged to duty, apparently well, on 26 February 1958.

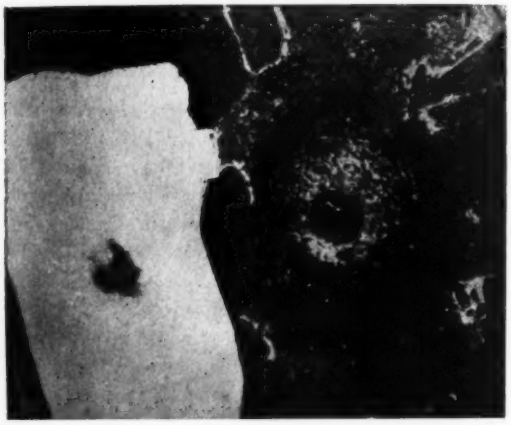

Figure 1 (case 2). Indolent coccidioidal ulcer on the thigh.

Comment

The results in this patient may have represented no more than the natural course of his disease. The distinct improvement in his skin and lungs during the course of therapy, however, was at lease suggestive that the drug was beneficial.

Case 3. A 27-year-old Negro was admitted to the hospital on 22 December 1956, complaining of cough. One month earlier he had noted the onset of bilateral chest pain and a cough occasionally productive of yellow sputum. One week before admission a painful swelling appeared on the left side of his neck. He had no fever, but did have a night sweat the evening before admission. He had lost 5 lb. in weight. He had been stationed in El Paso for two months.

On examination he did not appear acutely ill. His temperature was 98.6°F; pulse, 120; blood pressure, 112/70 mm hg; heighth, 70 inches; weight, 158 lb. There was a tender mass, measuring 3 to 4 cm in diameter, in the left supraclavicular fossa. A roentgenogram of the chest showed a linear infiltration in the left lower lung field, left hilar lymphadenopathy, and a soft nodular density in the left paratracheal region.

The coccidioidin skin test was positive. The white blood cell count was 11,700 per μl with 15 per cent eosinophils. The hemoglobin was 13.5 grams per 100 ml. *C. immitis* was cultured from the sputum. Complement fixation for coccidioidomycosis was positive in a dilution of 1:256. Biopsy

of the left supraclavicular mass showed a granulomatous tissue within which were many giant cells containing thick-walled spherules with endospores. Culture of pus from the abscess which appeared at the biopsy site was positive for *C. immitis.*

The patient's initial course was downhill. He had a low-grade fever, appeared moderately toxic, and became bedridden. He lost 33 lb. in weight during the first three months in the hospital. Six weeks after admission a tender fluctuant mass appeared over the right fifth rib just lateral to the midclavicular line. It measured 3 to 4 cm in diameter and 1.5 cm in elevation. *C. immitis* was cultured from pus obtained by needle aspiration of this abscess.

On 5 June 1957, intravenous therapy with amphotericin B was started. The initial dose was 15 mg daily for one week, 30 mg daily the second week, then 45 mg daily. On 21 June treatment was interrupted because of an elevated blood urea nitrogen. It was reinstituted on 28 June in doses of 30 to 45 mg every other day until 18 November when it was again stopped when the blood urea nitrogen was found to have increased. He invariably had nausea, vomiting, chills, and fever while treatment was administered. Acetylsalicylic acid and antihistamines were ineffective in controlling these reactions.

The abscess over the left fifth rib did not change in size from the time of its appearance in February until July. On 17, 23, and 29 July, it was drained through a large gage needle, and 20 mg of amphotericin B dissolved in 2.5 ml of water was injected into the cavity through the same needle. There was no evidence of any local irritation to the amphotericin B. The abscess decreased slowly in size and by 16 August had disappeared.

On 18 November the amphotericin, intravenously, was discontinued after a total dose of 2,550 mg over a six-month period. During the course of treatment the patient's general condition gradually improved. His strength and energy returned; the fever, except for that associated with administration of amphotericin, disappeared; he became ambulatory, and gained 15 lb. in weight. His complement fixation titer for coccidioidomycosis dropped from 1:256 to 1:64. He was discharged to duty on 13 December.

He was readmitted on 10 February 1958, complaining of pain in his neck and low back. There was straightening of the cervical and lumbar curves and spasm of the strap muscles in the same areas. Motion of the neck was limited. There was tenderness to percussion over the lumbar spine. Several small lymph nodes were palpable in the anterior cervical and inguinal areas. There was a crusted papular lesion, 1 cm in diameter, on the point of the right elbow. Roentgenograms of the lumbar spine showed an osteolytic lesion, 1.5 cm in diameter, in the body of the fourth vertebra.

Microscopic examination of a biopsy sample from the papule on the left elbow revealed characteristic findings of coccidioidomycosis, including the presence of the organism. The complement fixation for coccidioidomycosis was positive in a titer of 1:32. The lesion in the lumbar spine was presumed to be caused by coccidioidomycosis.

On 25 February amphotericin B, intravenously, was again started. The dose was rapidly increased to 50 mg every other day. The patient had chills and fever with each administration. In late March the drug was stopped for two weeks because of nitrogen retention. By 30 May, he had received an additional 1,890 mg of the drug, and a total of 4,440 mg intravenously. There has been no significant change in his condition on this last course of treatment and he continued to appear well except for the limitation in motion of his neck. His complement fixation had dropped to 1:16 in May.

Comment

This patient was severely ill and bedridden when amphotericin B was started. Improvement was noted coincidentally with the use of the drug. The evidence was suggestive that the drug was beneficial. Particularly notable was the rapid subsidence of the indolent abscess of his rib when injected locally with amphotericin. The appearance of new lesions of the skin and bone in February 1958 indicated continued dissemination in spite of the falling titer on the complement fixation test.

Case 4. A 22-year-old Negro was admitted to the hospital on 15 January 1958. In early December 1957 he had noted the onset of chills, fever, malaise, myalgia, back pain, nonproductive cough, anorexia, and a weight loss of 15 lb. He had been admitted to Biggs Air Force Base dispensary, El Paso, Tex., on 4 January 1958. There he was found to have fever, lymphadenopathy in the inguinal and anterior cervical areas, and a small papule over the right eye. His white blood cell count was 24,000 per μl, with 30 per cent eosinophils. He had been stationed in the El Paso area for 18 months.

Examination showed a thin, acutely and chron-

ically ill man who had lost a total of 25 lb in weight. His height was 68 inches; weight, 135 lb; pulse, 96; respirations, 30 per minute; temperature, 102.1°F; and his blood pressure was 140/87 mm Hg. There were numerous lymph nodes, measuring 2 to 3 cm in diameter in the anterior cervical, femoral, and inguinal areas. The liver was palpated 3 cm below the costal margin, and the spleen at the costal margin. There were scattered granulomatous skin lesions measuring 6 to 8 mm in diameter. There was one larger skin lesion over the right eyebrow, measuring 1.5 cm in diameter and 0.6 cm in elevation (fig. 2). A roentgenogram of the chest showed an infiltration in the right cardiophrenic angle and bilateral hilar lymphadenopathy.

Figure 2 (case 4) Coccidioidal granulomata on the face.

The white blood cell count was 20,550 per μl, with 10 per cent eosinophils. His hemoglobin was 11.8 grams per 100 ml. The coccidioidin skin test remained negative on monthly testing. *C. immitis* was cultured from the lesion above the right eye, from pus aspirated from an anterior cervical lymph node, and repeatedly from the sputum. Biopsy of the skin lesion above the right eye revealed a granuloma containing numerous thick-walled organisms with endospores. Complement fixation titer for coccidioidomycosis was 1:16.

Treatment with amphotericin B, intravenously, was initiated on 24 January. By 30 May, the patient had received a total of 2,970 mg in four months. The dosage eventually was stabilized at 50 mg every other day. The patient routinely had severe febrile reactions on each administration. On two occasions a rise in his blood urea nitrogen necessitated temporary cessation of treatment.

On different occasion, pus was aspirated thru a 16-gage needle from six enlarged fluctuant nodes in the neck, groin, and femoral areas, and 25 mg of amphotericin B dissolved in 2.5 ml of water was injected. Four were injected twice. There was no apparent local irritation to this procedure. Although he was receiving intravenous medication at the time, *C. immitis* was cultured from the pus from most of these nodes. All of the locally treated lesions decreased in size and became nonfluctuant over a period of 3 to 6 weeks after injection (figs. 3 and 4), but only one had completely disappeared.

Figure 3 (case 4). Coccidioidal abscesses in subinguinal lymph nodes shortly after they were first injected with amphotericin B.

His condition on admission was poor. He had a septic fever with a temperature of 103 to 104°F daily, and little appetite. About one week after admission he began to complain of severe pain in the left upper abdominal quadrant. On examination he had tenderness and rigidity of the abdominal wall in this area. There also was a partial paralytic ileus with considerable abdominal distension. This progressed to generalized abdominal tenderness and moderate ascites. A diagnostic abdominal paracentesis was not performed, but the

findings and course were thought compatible with coccidioidal peritonitis. The patient's condition appeared to be terminal at this time and he was carried on the seriously ill list. He had anemia severe enough to require four blood transfusions during his second month in the hospital.

In March, gradual and persistent improvement began. His ascites diminished, his appetite improved, and lymphadenopathy decreased, the hemoglobin stabilized at 10 grams per 100 ml and the skin lesions decreased in size. His fever continued, but the daily peaks were lower, 100 to 101°F. His strength returned and he was able to ambulate partially. No new lesions of the skin, lymph node, or bone appeared after amphotericin B was started on 24 January. The patient was far from well, but by May was much improved. In spite of the clinical improvement, his complement fixation rose from 1:16 on admission to 1:128 five months later.

Figure 4 (case 4). Same area shown in figure 3, two months after second injection of amphotericin B into abscess cavities.

Comment

This patient was moribund when treatment with amphotericin B was started. We were fearful that he would be unable to tolerate the toxic reactions to the drug. At the same time, the prognosis in a Negro patient with disseminated coccidioidomycosis of this severity is so unfavorable that it did not appear reasonable to withhold treatment. His improvement was not dramatic but it was impressive. Interestingly, his complement fixation titer rose as he improved clinically.

The cases presented differed in severity but were otherwise surprisingly similar. The following features were common to all four: Negro race, pulmonary symptoms at onset, fever, pulmonary infiltrations with hilar lymphadenopathy, early dissemination, marked weight loss, eosinophilia, sputum culture positive for *C. immitis*, complement fixation for coccidioidomycosis positive in dilution of 1:64 or more, peripheral lymph node involvement, abscess formation in peripheral nodes, and positive culture for *C. immitis* from the abscesses. Three patients had granulomata of the skin, two had a positive reaction to the coccidioidin skin test, two had bone lesions. One had anemia.

Our use of amphotericin B by mouth was limited to a short course of 38 days given to the first patient. Although the patient recovered, we were unable to draw any conclusions on this mode of administration.

Three patients who received amphotericin B intravenously reacted predictably with anorexia, nausea, chills, and fever on every administration. The reactions tended to decrease slightly in severity with continued medication, but remained severe after months of treatment. Salicylates and antihistamines were ineffective in our hands in altering the reactions. All three patients had an elevated blood urea nitrogen one or more times during treatment. This subsided on each occasion upon interrupting therapy for one or two weeks. Because of the unfavorable reactions, we were unable to exceed a dose of 50 mg (0.7 to 0.9 mg per kg), given over a six-hour period, every other day. This particular dosage may have been prompted to some extent by the packaging of the amphotericin B in 50-mg vials. Littman, Horowitz, and Swadey[2] independently arrived at the same conclusion as to frequency of medication, but were successful in giving larger doses. Our patients suggested that the infusions be started immediately after supper so as not to interfere with food intake. This was a useful consideration in treating a disease in which weight loss, malnutrition, and poor body resistance were important factors.

The results of treatment in a disease as unpredictable as disseminated coccidioidomycosis must

be accepted with caution. Our three patients improved while on intravenous amphotericin B therapy. It appeared likely that the favorable course of the disease was in part brought about by the drug. The response, if any, was slow. We were still able to culture *C. immitis* from a variety of areas in these patients after they had been treated intravenously with amphotericin B for months. We were unable to avoid speculating as to what might have been accomplished had we been able safely to give 10 or 100 times as much drug intravenously.

We injected amphotericin B into 7 coccidioidal abscesses, 1 in bone and 6 in lymph nodes. Two were injected once, 4 twice, and 1 three times, with about a week between injections. Positive cultures were obtained from nearly all of the abscesses, although the patients were receiving amphotericin B intravenously at the time. The dose was 20 to 25 mg dissolved in 2.5 ml of water. There were no untoward local or systemic reactions to the injections. All of the abscesses had been present for several months, and were either stationary or increasing in size when local treatment was started. The response was uniformly favorable. Two lesions healed completely in four to six weeks. The other five lesions decreased in size and became nonfluctuant in three to six weeks, but a residual firm mass remained. There seemed to be little doubt that the injection of amphotericin B directly into coccidioidal lesions was effective and useful. We believed that the relatively high concentration obtained in the abscess cavities explained the excellent response.

Smith[9] believed that the abdominal pain, partial ileus, and ascites in the fourth patient were manifestations of coccidioidal peritonitis. Retrospectively, diagnostic paracentesis and intraperitoneal injection of amphotericin B would have been desirable and possibly beneficial. At the time this report was written, the patient had improved to the extent that this measure was no longer under consideration.

The results obtained with amphotericin B intravenously indicated that is possibly was useful in treating disseminated coccidioidomycosis. The results obtained with direct injection of coccidioidal abscesses were more impressive. Amphotericin B in all probability represents the first real advance in the treatment of disseminated coccidioidomycosis, but further clinical testing will be essential. A similar agent with equal effectiveness but less toxicity could prove to be the answer to the therapy of coccidioidomycosis.

Four patients with disseminated coccidioidomycosis were treated with amphotericin B, one orally and three intravenously. The usefulness of the oral drug was not determined. The three patients on the intravenous preparation were treated for periods of 3 to 12 months. All improved while on therapy. Amphotericin B administered intravenously regularly caused chills, fever, anorexia, and nausea, during and shortly after each infusion. Salicylates and antihistamines did not alter these reactions. Azotemia occurred one or more times in each patient on intravenous therapy, but subsided upon interrupting treatment for one or two weeks. The unfavorable reactions were minimized by limiting the dose to 50 mg, given every other day immediately after supper. The water-soluble salt was dissolved in 5 per cent dextrose water to a concentration of 1 mg per 10 ml and infused slowly. Six hours or more were taken for each infusion.

Seven coccidioidal abscesses in two of the patients were injected directly with 20 to 25 mg of amphotericin B dissolved in 2.5 ml of water. Two were injected once, four twice, and one three times, the injections being about one week apart. The abscesses had been present for several months and were either stationary or increasing in size when injected. The response was uniformly favorable and fluctuation disappeared in three to six weeks.

Amphotericin B appeared to be an effective agent for the treatment of disseminated coccidioidomycosis. Its toxicity has limited the dosage, which, in turn, may have limited its effectiveness.

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Degree days yesterday, 4.*
Since Sept. 1, 4,885.
Normal since Sept. 1, 5,008.
Total last season to date, 4,667.
†The daily records of the U. S. Weather Bureau begin at midnight, Eastern Standard Time, or 3 A. M., Eastern Daylight Time.
*A degree day (for heating) is the technical term for the number of degrees the mean temperature falls below 65. The American Society of Heating Engineers has designated 65 as the point below which heating is required.

POLLEN COUNT

Daily pollen counts compiled for information of hay fever sufferers and physicians are shown below. Each count represents the average number of pollen particles per cubic yard of air in the 24-hour period. The following table shows counts for the last seven days.

Tuesday	17
Wednesday	42
Thursday	61
Friday	78
Saturday	25
Sunday	47
Monday	79

The Summary

Showers and thunderstorms continued yesterday from southern Virginia and the eastern Tennessee Valley southward into Florida, and in the Gulf States and Texas. There were thunderstorms in the Rockies and the western parts of South Dakota, Nebraska and Kansas.

A warming trend was reported in the Pacific Northwest, the Northern and Central Plains States, eastern Wyoming and Colorado and the Tennessee Valley. Cool dry air covered New England and Minnesota.

An area of high pressure will cover the middle Mississippi and Ohio Valleys this morning. The rest of the country will be under the influence of low pressure. A trough will extend from the North Carolina coast southward through the South Atlantic States to a low-pressure center in the Gulf of Mexico and then curve northwestward through the Plains States to southeastern Montana. Other low-pressure centers will be off the northern California coast, in Nevada and just north of Montana.

Scattered showers and thunderstorms are forecast for today in the Gulf States, southern Georgia, South Carolina and Florida. The northeastern quadrant of the country will be sunny, except for southern Maryland and eastern Virginia which may have rain. Thunderstorms are predicted for the higher Sierras, the Rockies, the Central Plains States and western Texas. A warming trend will be observed in the upper Mississippi Valley, the eastern Dakotas and eastern Nebraska.

The Forecast

United States Weather Bureau.
(As of midnight.)

NEW YORK CITY, LONG ISLAND AND

Bath Oil in the Management of Senile Pruritus

By ARTHUR R. P. JAMES, M.D., Dermatologist to St. Vincent's, Toledo, Mercy, St. Lukes, Children's and Maumee Valley Hospitals, *Toledo*

The incidence and severity of pruritus increases markedly with age. Atrophic changes in the cutaneous and subcutaneous layers cause the skin to be thinned. The cuticular appendages (sweat and sebaceous glands) decrease in function so that the skin surface becomes dry, flaky, and tends to fissure more easily. There is a definite reduction in the oil and water content of the stratum corneum. Degeneration of the elastic and collagen tissues and involvement of the nerve endings are also probable important factors in this type of pruritus.

The conditions initiating the discomfort will vary from case to case. Commonly, changes in room temperature or humidity will cause trouble and many cases complain of severe itching at bedtime. However, by far the commonest statement is "I can't tolerate a bath; soap and water irritates me and makes me itch." Practically all cases are worse during cold weather. Senile pruritus tends to become progressively worse as the patient gets older.

Differentiation

In the evaluation of the individual case it is essential to determine all the possible factors to be certain that one is dealing with "Essential Senile Pruritus" **per se** and not with itching due to systemic disease. Other factors such as pediculosis, scabies, insect bites, etc., may be etiologic and should be considered. Irritating contactants should not be overlooked. In many cases we find very extensive excoriations due to acarophobia.

Adequate consideration of the history, physical examination and routine laboratory examination should rule out systemic disease. Disease of the liver and its ducts, with bile salts in the blood, will cause intense pruritus and since carcinoma is often a factor in the etiology of jaundice, one would expect to see this type of skin itching more frequently in the aged. Carcinoma itself may cause pruritus of obscure etiology. Any one of the lymphoblastomas may cause intense pruritus.

Therapy

In the treatment of senile pruritus the most important endeavor is to return to the dry skin the oil and water which it lacks. In limited areas of dry skin, optimum results are obtained with lotions or creams which can lubricate the skin and supply it with moisture. They should be occlusive enough so that the moisture thus supplied to the skin can be retained for relatively long periods. We have observed excellent results from an emollient cream* containing a new keratin-soluble, de-waxed liquid fraction of lanolin.

However, where extensive areas of skin are itchy and dry, the use of emollient creams should be supplemented with the use of bath oils. While the use of bath oils is not new in dematology, they were not widely accepted because of their poor dispersibility in water. Knox, Everett and Curtis[1, 2] pioneered in developing more therapeutically effective and cosmetically elegant bath oils by suggesting incorporation of low sensitizing, non-irritant, non-ionic surface active agents into vegetable and mineral oils. During the past two years a clinical evaluation of bath additives has revealed the most satisfactory to be a combination* of the new keratin-soluble, de-waxed liquid fraction of lanolin (above), a non-ionic emulsifier (polyethylene glycol laurate), mineral oil and a synthetic perfume of low sensitizing quality.

Solves Problem

It is interesting to note that the use of this bath oil, in senile pruritus cases, solves the difficult problem of cleansing the skin without the use of soap, soap substitutes and colloid or oat-meal baths which are often irritating. The patients are instructed to add one-half to one ounce of the oil to the tub of lukewarm water and to soak in the tub for five to twenty minutes. This provides adequate cleansing of the skin and leaves a thin film of emollient, moisture-retaining oil on the keratin.

In the management of senile pruritus it is possible to establish a routine and to modify or add to it as warranted by the individual case. If the pruritus is severe at the time of the initial visit, it may be necessary to prescribe a tranquilizer and temporary sedation. For short periods of time bromides are the sedative of choice. Anti-pruritics such as camphor, phenol and menthol may be used in Nivea Oil or a suitable ointment base to bring the acute condition under control. Occasionally it may be advisable to add tar in the form of Wright's Liquor Carbonis Detergens,

#Aquasol "A"—U. S. Vitamin Corp.
†Nivea Oil—Duke Laboratories, Inc.
*Alpha-KERI Oil and Lowila Emollient were supplied by Westwood Pharmaceuticals.

drams one to each ounce of the topical application. The patient is instructed to take 50-100,000 units of Aquasol "Vitamin A" daily.

Frequent soothing tub-baths with alpha-KERI Oil are suggested. Once the condition has been brought under control, topical anti-pruritic applications are discontinued and the patient is advised to apply Lowila Emollient to the skin as desired and to continue with use of the oil in the bath.

Results

The results of the investigation are outlined in Tables I and II which include cases of senile pruritus as well as other dermatoses wherein the soothing, anti-pruritic effects of the bath oil have been found of adjunctive value to treatment.

Typical case histories for senile pruritus and ichthyosis are as follows:

CASE 203 — This 85-year-old white male has been under therapy since 1945. His complaint was itching of the skin aggravated during the winter. Soap and water increased the itching which had progressively become worse. Adding oatmeal and corn starch to the bath water was of little help. By 1953, the condition was so severe he was afraid to take a soap and water bath during the winter and resorted to cleansing his skin daily with olive oil.

At the time of his first visit he was told to take Aquasol "A"; 100,000 units daily; and to use Nivea-Oil.† He was given an anti-pruritic ointment containing Camphor, Phenol and Menthol to control his pruritus. In April, 1957, alpha-KERI-Oil* was made available. At that time, his skin condition was very severe. It took much persuasion to overcome his fears and induce him to take a tub-bath with the added oil.

The results were excellent and he has continued to take the baths regularly with very little itching of the skin. After the bath he applied Lowila Emollient* to his hands, arms and legs. He rarely has to use the anti-pruritic ointment.

CASE 487 — This 42-year-old white male was first seen Aug. 2, 1958. He represented a moderately severe case of ichthyosis. He stated that the discomfort was severe in the cold weather. His general examination and laboratory studies were not significant. He claimed that he cleansed with olive oil most of the time because soap and water baths irritated his skin. He was told to take 50,000 units of Vitamin "A" twice daily. He was given the bath oil for his tub-baths and told to apply Lowila Emollient often during the day. He claims this type of management has afforded him remarkable relief. He enjoys a daily bath with the oil and his response to therapy has been satisfactory.

TABLE I
RESULTS IN SENILE PRURITUS

No. of Cases	Male	Female	Ages	Avg. Age	Gd.	Fair	Did Not Like	Couldn't Use
186	122	64	Oldest 86 years Youngest 46 years	57	161	19	6	0

TABLE II
RESULTS WITH ALPHA-KERI IN OTHER DERMATOLOGICAL CONDITIONS

Condition treated	No. of Cases	Male	Female	Clinical Evaluation of Results: Good	Satis.	Fair	Not Tol.
Eczematoid Derm. Infectious	14	10	4	1	8	5	
Allergic	46	22	24	9	30	6	1
Derm. Venenata	465	222	243	203	198	64	
Psoriasis	56	30	26	7	30	19	
Seborrheic Derm.	23	14	9	10	9	4	
Derm. Herpetiformis	4	4	....	....	4	....	
Urticaria	21	13	8	3	10	8	
Drug Eruptions	11	4	7	3	5	3	
Ichthyosis	7	5	2	7	....	....	
Stasis Derm.	13	8	5	6	6	1	
Pruritus Vulvae	19	....	19	9	10	....	
Ani	41	29	12	25	16	....	
Winter	3	3	....	3	....	....	
Bath	5	3	2	4	1	....	
Miscellaneous Pemphigus, etc.	44	23	21	6	25	12	1
TOTALS	772	390	382	396	352	122	2

Summary

Senile pruritus is probably the most common skin affliction of the aged. Its treatment should take into account the many and varied etiological factors described.

Soap and water aggravate the itching. It has been observed that a satisfactory method of cleansing the skin is the use of the new bath oil additive described. This provides a soothing, anti-pruritic soak of definite adjunctive value to more specific treatment.

Results of these soothing, anti-pruritic cleansing baths were considered good in most cases with senile pruritus and pruritus due to other dermatoses. The incidence of intolerance or sensitivity was less than one per cent.

2140 Scottwood Avenue.

References

[1]Knox, J. M.; Everett, M. A., and Curtis, A. C.: New Uses for Surface-Active Agents, A.M.A. Arch. Dermat. 74:699-706 (Dec.) 1956.

[2]Knox, J. M.; Everett, M. A., and Curtis, A. C.: A.M.A. Arch. Dermat. 78:642 (Nov.) 1958.

MONTHLY CLINICAL PATHOLOGICAL CONFERENCE
EL PASO GENERAL HOSPITAL

March 19, 1959

F. P. BORNSTEIN, M.D., *Editor—Case 1199*

Presentation of case—Dr. John Verosky

History — Dr. Nathan Kleban:

On Dec. 2, 1958 a six lb. 2½ oz. boy was born to a 17-year-old girl, her first pregnancy and first child. Pregnancy was said to have been free of complications. Respiration and cry occurred two minutes after resiscitation was started. Physical examination impression was "a normal newborn." It was stated that the infant's condition appeared good on Dec. 5, day of discharge.

Because of cyanosis and poor eating for one week, the infant was re-admitted on Dec. 22.

Physical Examination:

There was generalized intense cyanosis. Clubbing was not present. Radial and femoral pulses were equal. Neck veins were slightly full. There was no chest deformity. Three nipples were present on the right. PMI was at xiphoid. A grade III murmur, medium to high in pitch, slightly crescendo in early and mid-systole, was most intense at the fourth left intercostal space and transmitted along the left sternal border to the base. S-1 was split, maximal at xiphoid. S-2 was not split, maximal in the second left intercostal space. Flush systolic blood pressures were: right arm 60, left arm 80, right leg 40, left leg 90. Liver edge was 3-5 cm. below the right costal margin.

Hospital Course:

Maximum temperatures ranged from 99 to 100. Weights on the seventh, eighth and tenth days were, five lbs. 14½ oz., six lbs. three oz., six lbs. Pulse before digitoxin was 148, later slowed to 104, but again went up to 148. Productive cough was noted on the 20th day. Despite chloramphenicol, nystatin, oxygen, digoxin, and mercurial diuretic, cyanosis persisted, respirations remained labored, and the baby died on the 22nd hospital day.

Laboratory Findings:

X-rays: 12-23-58: Radiographic examination of the chest reveals the lungs to be well ventilated. There are bilateral intensifications of the pulmonary markings suggestive of congestive failure. The contour of the cardiac silhouette is consistent with congenital heart disease, possibly a tetralogy. The bony thorax and diaphragm are otherwise intact.

12-31-58: As compared to the examination 1 week ago, the appearance of the chest is not changed significantly, still showing the abnormal cardiac configuration and pulmonary vascular congestion.

Blood counts: 12-23-58: Hb. 14.8 gms., Ht. 44 vol. %, WBC 18,000, Stabs. 5, Segs. 60, Lymphs. 33, Eosin. 2 (9 nucleated rbc). 1-5-59: Hb. 8.0 gms., Ht. 25 vol. %, WBC 9,000, Stabs. 3, Segs. 45, Lymphs. 52. 1-11-59 — Hb. 16.0 gms., Ht. 48 vol. %.

Urinalysis: 12-23-58 — S.G. QNS, straw, clear, acid- albumin and sugar negative, many sq. ep. cells.

Throat cultures and sensitivity: 12-23-58 — Monilia and Neisseria sp. Sens. Erithromycin, Penicillin, Tetracycline. 12-31-58 — Staph. and pneumococcus — Sens. Erithromycin, Penicillin, Tetracycline. 1-5-59 — Staph. and pneumococcus — Sens. Erithromycin, Penicillin, Tetracycline. 1-13-59 — Neisseria sp. and Strept. Sens. Erithromycin, Chloromycetin.

Electrocardiograms — 12-23-58—Extreme right heart enlargement (relatively). 12-27-58 — Right heart prominence.

X-Ray Discussion — Dr. Charles McVaugh:

On the original examination of the chest the lateral shows more unusual findings than the P-A. There is an enormous heart shadow which has displaced the trachea posteriorly. In the intervening eight days there is no change in the heart size. I think it is a very large heart but I cannot say definitely whether the right and left ventricles or both ventricles are enlarged. I think it is mostly the right ventricle because of the upward displacement of the apex of the left heart border. I think, then, this is largely right ventricular enlargement. I can't identify the aorta. If this child had a coarctation I can't determine it. (Fig. 1)

At the original examination the lungs were well expanded bilaterally. In addition there is a definite increase in the pulmonary vascularity. I think this increased vascularity is due to a left to right shunt rather than to congestive failure. In the intervening eight days there have been some changes in the lung fields, namely, an increase in the pulmonary vascularity. Maybe that is because of some congestive failure beginning to

occur on top of the increased blood flow. There is no particular enlargement of the liver. In summary, I think this is a left to right shunt with enormous right ventricle. That is all I can say.

Clinical Discussion: — Dr. John Verosky:

I might want to refer to these X-rays later on. The problem before us is the diagnosis of a congenital heart lesion in a young infant. This is entirely a different problem than the diagnosis in the child or young adult. In the latter the findings are usually so well defined that one can make an exact clinical diagnosis.

In the child and adult one is ordinarily able, using the physical findings (particularly those of auscultation of the heart), the electrocardiogram and X-ray to make an anatomic and functional diagnosis in over 90 per cent of cases.

Now in the young infant this is not true. We are able to make an exact anatomical diagnosis in less than 50 per cent of the cases.

We attempt to do only two things: first, we attempt to place the infant in the proper subcategory of congenital heart lesions, and second, and much more important, we attempt to handle the patient in such a way that we do not unnecessarily risk the life of a young infant who might survive to an older age by dangerous diagnostic procedures. At the same time, we try to avoid allowing the infant with an operable lesion to die without the benefit of surgery.

The reasons for the difficulty in the diagnosis are manifold. The most disconcerting one is the lack of distinctive physical findings. The X-ray can let you down too, it is amazing how frequently in the first month of life it is difficult to be sure one way or the other the size of the heart. The involved physiological investigations are not simple, either.

In the first place, they have to be done under more or less general anesthesia, or at least under deep sedation. If you are going to do such difficult procedures on a little baby, it means of course that the infant is quite ill, so what one has, in effect, is general anesthesia and a very sick baby; hence the hazard of catheterization, angiocardiography and so forth, is considerably higher than we accept in a five-year-old, or ten-year-old child.

The testing itself is difficult; the veins are small; small catheters must be used; there are many artifacts; general anesthesia itself produces artifacts; and so the whole thing is difficult, from a clinical and from an investigative point of view. Fortunately, or unfortunately, depending on one's point of view, this is of no great significance at the moment, but this is a strictly temporary situation. The reason that it is of no vast significance is that most of the lesions that cause death at an early age are, today, inoperable. This is a very temporary situation. Looking back on the advances in heart surgery in the last ten years, it is quite predictable that in five years, perhaps less, almost all congenital hearts will be operable; then the cheese will be more binding, and it will be imperative to make exact diagnoses on a high percentage of these babies because a high percentage of them will be salvagable.

Several Aids to Diagnosis

There are several aids, though, when one attempts to make a diagnosis. One of the reasons that diagnosis is so relatively simple in the older age group, is that most of the complex and highly lethal anomalies have already died. We know that if a patient is 15-months-old, he cannot, for instance, have an anomalous left coronary artery because none has ever lived that long; but such an assumption in a one month old baby is invalid.

On the other hand, I have one distinct advantage here tonight. This baby died. There is an entirely different choice of possibilities when one is looking at an infant of this sort alive, as compared with the possibilities when one knows the baby expired, because there are only a certain number of these defects that are serious enough to cause death at that age. So as soon as the patient dies, one has an added advantage. This is a very helpful factor.

In reviewing the protocol, I note one omission; the baby was born here. The newborn record describes a perfectly normal baby. Now does this mean that somebody didn't listen well, or didn't notice cyanosis? Not at all. None of us can take care of newborn babies very long without this same thing happening to him. A baby that is signed out as perfectly normal will return and die in a month or two with a congenital heart.

Many of these fantastically severe anomalies do not produce cyanosis in the first week, and nowadays most babies go home in five days. A great many of them produce no symptoms, and no murmurs. So the doctors running the nursery should not feel put out that they missed a possible congenital heart, because it has happened to all of us. It has certainly happened to me.

Now the patient was cyanotic at about a week of age. One notes the poor growth, that many of

the severe anomalies produce. The patient was not clubbed. Clubbing takes a certain amount of time for its production, so this is not too remarkable. There is no chest deformity.

As you know, if the left chest is very prominent, we assume right ventricular enlargement (dilatation, or dilatation and hypertrophy). This patient did not have chest deformity. This does not mean the right ventricle was not large, because there are several factors necessary in the production of left chest deformity.

You must have a big right ventricle and you must have it for a certain amount of time in a growing chest and this baby hasn't grown. So without growth you cannot get a nice prominent left chest that one gets in the older child with right ventricular enlargement. The point of maximal impulse was at the xiphoid which again points to relative preponderance of the right ventricle.

There were three nipples. I don't know just what one can make of that because we certainly see multiple nipples in lots of children, but I think in the newborn nursery if you see three nipples, you should look a little harder for congenital anomalies. The murmur, the details of which we won't repeat, add up to ventricular septal defect.

However, in complex anomalies ventricular septal defect occurs in all sorts of situations; ductus arteriosus, transposition, tetralogy of Fallot, etc., etc. It does not mean that there is a plain ventricular septal defect. It means that a ventricular septal defect is probably present. This is not terribly helpful because of the commonness of ventricular defects as an additional anomaly with many more complex anomalies.

The heart tones are of note in that the second sound is unsplit. The normal infant beyond the newborn stage and the young child always have a second sound that is normally split, and this one was unsplit. Now, in the nursery, in the first couple of weeks of life, splitting can be so close that it can be pretty difficult to hear. So since this baby was only three weeks old, one has to remember that factor. But suppose it were validly unsplit; there are several things that will produce an unsplit second sound.

The stenotic semilunar lesions (pulmonic stenosis and aortic stenosis) can, although not necessarily invariably, produce a pure second sound. Truncus arteriosus can do the same since there's only one valve, but it is surprising how often a truncus can have a split second sound.

The reason for this is beyond me. There are usually four or five leaflets and perhaps they don't close with the same synchronous timing as do the three leaflets of an ordinary semilunar valve. If there is aortic valve atresia, one can also hear an unsplit second sound. Then another one is transposition of the great vessels. This is a positional thing.

Normally the great vessels and semilunar valves lie side by side. In transposition they tend to be related anteriorly-posteriorly so that the one that is behind may be so far away that one might not hear it. So there are quite a few possibilities that can give us an unsplit second sound.

The blood pressures are normal. At least one leg was higher than the arms. This is very helpful in this sort of baby, because it means that we can probably eliminate most of the aortic arch anomalies that involve hypoplasia of the arch with relative hypertension in the arms, the so-called infantile coarctations.

There is evidence of failure. This is significant. There are several different causes why little babies die of congenital heart disease, only one of which is congestive failure. Probably just as common is anoxia, for instance in pulmonary atresia or severe tetralogy. But this was failure. The liver was large, the neck veins were distended. It is difficult to see this distention in a little infant, but this baby actually had some.

Now on the X-rays I would like to make some comments if I may, Dr. McVaugh. I certainly agree that the pulmonary vascularity is grossly increased. This does not mean left to right shunt. It means the pulmonary vascularity is grossly increased. The heart is big. The cardio-thoracic ratio works out to be about .65 which is not terribly big, but it is big.

That is about the limit of the accurate information one can obtain from a chest X-ray of an infant with congenital heart disease. Those two things—the size of the heart and the state of the pulmonary vasculature. Is the vasculature normal, increased or decreased? It is very difficult to go beyond that. Anything else is guessing, but let's guess that the right ventricle is large, and that there is probably some enlargement of the right atrium.

This is pure guesswork, but it does look that way a little bit. The other thing that impresses me is the narrowness of the pedicle of the great vessels in the P-a view. I believe that there is considerable suggestion that the great vessels run-

ning into the base of the heart are larger on the lateral than they are on the P-a. It is a debatable thing, however.

The electrocardiograms, the details of which are not in the protocol, showed several interesting things. The P-wave was peaked in Lead II and Lead V-1 and up to about 3½ mm. in amplitude. This represents right atrial enlargement. The right ventricular hypertrophy was extremely marked. The T-wave in V-1 was upright, which beyond 48 hours and before one year of age means right ventricular hypertrophy even if you find nothing else. There is in addition, however, a 28 mm. R-wave in V-1 — absolute top normal is 25. The R prime wave in AVR was 12 mm., top normal on that at this age is six.

To summarize, then, we have a cyanotic child with increased vascular markings, with right ventricular hypertrophy. Of those things we can be very sure. In addition we have a baby who was very sick, who died at a young age, who died of congestive failure, who has a ventricular septal defect murmur, and who has an unsplit second sound.

Now, how can we put these things together? Well, in a way there are two types of diagnoses in medicine. First there is the analytic one, very much similar to the process one went through in qualitative chemical analysis, where the metals are divided into groups and one precipitates this and that with acids and so forth, a very deliberate and logical series of deductions.

Then there is the Aunt Minnie type. Do you know what the Aunt Minnie type is? Well, a few years back Dr. Ed Neuhauser, one of the world's most renowned pediatric radiologists, was giving a series of lectures in pediatric X-ray in Cincinnati, Ohio, and at the end of each lecture session the local radiologists and residents would get their meanest films, their toughest diagnoses, and flash them up for him to guess; one of these times they flashed up a film and said, "This baby is a week old"; and he said "This is Wilson-Zeulzer disease" (complete absence of the myenteric plexus in the entire colon).

There was a pause, and a vast silence — of course he was right — and one of the local men got up and said, "Well, Dr. Neuhauser, how did you know that?" He replied, "Well, I have an Aunt Minnie, and if I see her walking down the other side of the street I don't have to go over to her or see how tall she is, I just wave and say, "Hello, Aunt Minnie". This is Wilson-Zeulzer's disease because I've seen it before and that's what it is." There are some types of congenital heart that one can diagnose on the Aunt Minnie basis, such as a clear cut, six-year-old child with a patent ductus with every finding in the book; but in a situation such as our present one one should not do that.

One should be far more deliberate and analytic in one's approach. We have indicated before that our chances of being correct in this process are no greater than 50 per cent as far as the exact anatomical procedure, but that we can usually, (unfortunately not always), decide which infant is worthy of dangerous testing. This is the procedure which should go through one's mind.

We divide congenital hearts by three procedures into groups, the first of which is the presence or absence of cyanosis. This is the chemical definition, not the clinical one, because it is amazing how cyanotic a child can be without one being aware of it. Chemical cyanosis means that the child's oxygen saturation in the arteries is less than 92 per cent. Those that are over 92 per cent we divide into three groups: those with normal pulmonary vasculature, those with increased pulmonary vasculature, and those with decreased pulmonary vasculature.

Of those with normal pulmonary vasculature, all the significant ones have left ventricular hypertrophy, and there are three groups. We put them down as items but each of these comprises a number of diseases. The first one is coarctation of the aorta. We are putting the percentage of incidence down because this is very important in one's guesswork. Six per cent of all congenital hearts have coarctation of the aorta.

Then we have aortic and sub-aortic stenosis which is a surprising four per cent, and finally we have a group of diseases, the primary endomyocardial diseases, which are about one per cent, which include a whole host of things, the most well known of which are endocardial fibroelastosis, anomalous left coronary artery, the congenital myocardial degenerations seen with muscular dystrophy, Friedreich's ataxia, etc.

In those who have increased pulmonary vasculature and are not cyanotic, we have two groups, those with left ventricular hypertrophy and those with right ventricular hypertrophy. Under left ventricular hypertrophy we have two: patent ductus arteriosus (17 per cent) and ventricular septal defect (22 per cent). Of those with right ventricular hypertrophy we have ventricular

septal defect with pulmonary hypertension which constitutes about three per cent atrial septal defect (the secundum type of defect) that constitutes about seven per cent, the foramen primum or perhaps better called the endocardial cushion defect which constitutes two per cent and isolated partial anomalous pulmonary venous drainage which constitutes far less than one per cent.

Then in those with decreased pulmonary vasculature we only have one which has right ventricular hypertrophy—isolated pulmonic stenosis, valvular or infundibular. So if the patient is not cyanotic he belongs here. Now this classification must be taken with much salt. Patients shift. They develop pulmonary hypertension and change from left ventricular hypertrophy to right ventricular hypertrophy. If the hypertension gets bad they get cyanotic and they go on the other side of the board, and so forth, but in a general way most of them can be made to be fit in with this.

Now of those who are under 92 per cent, the cyanotic ones, we have those with increased pulmonary vasculature and those with decreased pulmonary vasculature. Of those with increased pulmonary vasculature, all have RVH, and under this there are five main sub-groups, the most important of which is transposition of the great vessels which constitutes about eight per cent of all congenital hearts.

We have complete anomalous pulmonary venous drainage which constitutes again an amazing two per cent. We have the aortic atresia group that has probably best been described by Ler as the hypoplastic left ventricle group. This includes a number of diseases the whole of which add up to about two per cent. Then further we have truncus arteriosus which constitutes less than one per cent, and finally we have single ventricle when the single ventricle is without pulmonary stenosis which constitutes something over one per cent.

Of those cyanotic individuals with decreased pulmonary vascularity, we have two groups, those with LVH and those with RVH. Under LVH we have two, tricuspid atresia which constitutes three per cent and finally Epstein's disease which again is rare and is less than one per cent. Under right ventricular hypertrophy of course we have Tetralogy of Fallot which constitutes eleven per cent, pulmonary atresia which constitutes one per cent, and single ventricle with pulmonary stenosis.

Our baby is cyanotic, it has increased pulmonary vasculature and it has right ventricular hypertrophy. We will take first single ventricle without pulmonary stenosis. Single ventricles come with and without pulmonary stenosis. Those who have pulmonic stenosis are blue—very blue, and have a good life expectancy.

They do not die in early infancy. Those without pulmonic stenosis have tremendously flooded lungs and usually die at this age, but they are not this blue. For that reason I think we can eliminate this, because really blue single ventricles are those who have pulmonary stenosis. You see how heavily we go on statistics.

Next we have the group of the hypoplastic left ventricle. This is a group of six diseases, the most common of which is aortic valve atresia and aortic arch hypoplasia. The latter is what is sometimes called infantile coarctation. Then we have mitral atresia, mitral hypoplasia, mitral stenosis and combinations of these. These babies die early, particularly the aortic valve atresias, the aortic hypoplasias and the aortic atresias.

There have been several of these in town lately and I think you will all agree that what usually happens is that the baby very suddenly gets sick and dies in congestive failure, but for the degree of failure they are not this blue. This baby was markedly cyanotic.

These babies are pale, sick, and dyspneic and have poor peripheral tone, poor peripheral pulses and often clues such as the difference in pressure in the arms and legs with the aortic arch hypoplasia group, but they don't look this purple until an hour or so before they die.

Here is a baby that was on our ward about two weeks before it finally died, two weeks during which it was bright blue, so there is again too much cyanosis for this. Then we have truncus arteriosus.

There are again two classes of truncus arteriosus, one in which the pulmonary arteries come off the trunk and one in which there are almost no pulmonary arteries in the lungs and the lungs are supplied mainly by the bronchial arteries and we have the same distinction that we saw in single ventricle.

The ones with arteries coming off the trunk are not terribly blue but are awfully sick and die young. The ones with the big bronchial arteries are very blue but are not as sick and are apt to go on for several years; they do not typically die at this age.

Again you see what an advantage it is to know that the baby died. Now also in the bronchial artery group where the blueness is this intense

one will usually find the continuous murmur of very large bronchial arteries over the back. This baby did not have this, so neither fits our baby.

Then we have total anomalous pulmonary venous drainage. There are four kinds of those. In one, the veins join an anomalous left superior vena cava to give a very characteristic X-ray picture called variously the snow man shadow, figure of eight shadow and a few other names, in which one has the heart and then over it a shadow almost as big, that is the tremendously dilated caval system.

The baby didn't have that. As a matter of fact the vascular pedicle is narrow. These babies, incidentally, do not die this young, but are very blue. The second type includes those joining the right atrium or coronary sinus, which physiologically adds up to the same thing. These babies again do quite well, they do not die at this age, although they are very blue.

The third group are those joining below the diaphragm, sub-diaphragmmatic ones joining the portal system; these babies are terribly sick and die very early, but there is one finding that is quite characteristic in these babies and that this baby did not have, and that is a triple or quadruple rhythm. In addition, almost all of these babies have well developed diastolic murmurs; our baby had no diastolic murmur.

The fourth type are combinations of these three. So we find on analysis here that none really fits our baby.

Finally we have transposition of the great vessels, which is the only one that really fits. Transposition of the great vessels is suggested in a baby of very young age who is very blue, has congestive failure and has severe right ventricular hypertrophy; a ventricular septal defect is very possible with this. The X-ray is suggestive, but not terribly diagnostic. In transposition the pulmonary artery and the aorta are one in front of the other and one gets a very narrow pedicle. On the lateral one separates the two vessels and the pedicle widens.

I think in the first film one gets the idea of an egg shaped heart, also suggestive of transposition. If he has transposition of the great vessels, the fact that he lived a month means that he had some sort of shunt, between the pulmonic system and the systemic system, otherwise the baby would never have lived extra-uterinely.

There is some correlation between the age of survival and the amount of shunting but the correlation is not perfect; in a general way the more the shunt the longer these babies live; one of the older operations for this disease is to create an atrial septal defect, increasing the mixture between the pulmonary circuit and the systemic circuit—an operation which doesn't work very well.

On the other hand one has an occasional baby with a ductus, with a foramen ovale and a ventricular defect that dies in the first week, so the correlation is not good, but again we have to go by statistics in a thing like this and one would say that the baby dying at less than a month of age probably does not have much in the way of shunting.

We know the baby has a ventricular septal defect from the stethoscope so I would think that that is all the baby has, transposition of great vessels with a ventricular defect, because the odds are that if the baby had more shunting (perhaps on atrial communication and a patent ductus) the baby probably would have survived a little longer.

Taussig used to say in her first book that the reason transpositions look so well when they are born and all of a sudden fall apart a week or a month later, is that the ductus closes; the ductus which could stay open to save the baby's life inexorably goes ahead and closes, and that is when the baby gets into severe difficulty with a decrease in the admixture of the two circulations, and so the baby deteriorates rapidly.

I don't know whether this is so or not but actually it isn't too bad a theory. There must be some reason why these babies are pink for the first week of life. In addition the baby probably had pneumonia; most babies in failure who die do have bronchopneumonia.

What we try to do is not make an exact diagnosis, because we know our batting average on that is poor. What we attempt to do is put the baby first in the proper category; in other words, in the major divisions using the aids of the pulmonary vasculature, cyanosis or absence of same, and the right or left ventricular predominance. In each sub-group we try to decide if the baby has a chance of having something operable, so as not to let the baby die without the benefit of some sort of heroic surgery; we hope that we have at least accomplished that in this baby.

Clinical Diagnosis: Congenital heart disease.

Dr. Verosky's Diagnosis: Transposition of great vessels.

Pathological Diagnosis: 1. Complete transposition

Figure 1

of large blood vessels with nearly complete occlusion of foramen ovale and atresia of ductus arteriosus. 2. Minimal interventricular septal defect. 3. So-called myxoma of heart.

Pathological Discussion—Dr. F. P. Bornstein:

I am supposed to say at this point that the case is open for general discussion, but I don't know what is left to say. I am baffled by what Dr. Verosky meant when he said he wasn't trying to make an exact diagnosis.

On autopsy there were three nipples as mentioned before. On opening the thorax with the pericardium intact the cardiac hypertrophy was quite obvious. On dissection of the heart it was easy to demonstrate a complete transposition of the large vessels. The aorta was easily identified as coming out of the right ventricle with the presence of coronary ostia.

The pulmonary artery arose from the left side. The pulmonary artery, the left ventricle, the ductus arteriosus, all three were extremely hypoplastic and there was obviously a progressive closure of the ductus arteriosus which produced the fatal result.

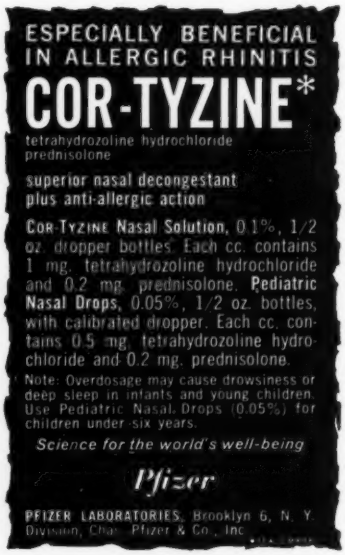
Tiny Interventricular Septal Defect

There was an extremely tiny interventricular septal defect under the tricuspid valve. In addition there was a bronchopneumonia. There was one additional finding which only rates as an

Figure 2

oddity. Located at the tricuspid valve was a peculiar tumor-like lesion (Fig. 2), a so-called congenital myxoma of the heart. There is considerable controversy about the interpretation of these tumors. Some people think they represent organized thromboses and not tumors at all, but this child was too young to have a mass develop on this basis.

This, then, is a classical example, as Dr. Verosky predicted, of complete transposition of the large vessels with a small ventricular defect, a progressively narrowing ductus arteriosus and a bronchopneumonia.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Note: Overdosage may cause drowsiness or deep sleep in infants and young children. Use Pediatric Nasal Drops (0.05%) for children under six years.
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